

## **REMARKS**

The Office Action dated January 2, 2004, has been received and reviewed. Claims 25, 27 and 29-33 are pending in the present application. Claims 34-35 have been added. Claims 25, 27 and 29-33 stand rejected. Applicants have canceled Claims 25, 27, 29-31 and 33. Applicants respectfully request reconsideration of the application in view of the arguments below.

### **I. Claim Amendments**

Claim 32 has been amended. The amendments are merely cosmetic in effect and do not alter the scope of the claimed subject matter. Support for these claims can be found throughout the specification and figures, particularly on pages 3-4 of the present specification.

### **II. Rejections under 35 U.S.C. § 112, second paragraph**

Claim 33 stands rejected under 35 U.S.C. § 112, second paragraph. Applicants have canceled this claim thus mooting this rejection.

### **III. Rejections under 35 U.S.C. § 102(b)**

Claims 25, 27 and 29-31 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Martin et al. (WO 00/74684A1). Applicants have canceled Claims 25, 27 and 29-31 thus mooting this rejection.

### **IV. Rejections under 35 U.S.C. § 103(a)**

Claims 32-33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kaken Pharm Co. Ltd. (JP 10279483) (hereinafter "Kaken") in view of Borah et al. (EP 0322020). Applicants traverse this rejection for the amended claims for the reasons set forth below.

To establish a prima facie case of obviousness, the prior art reference or references when combined must teach or suggest *all* the recitations of the claim, and there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143. The mere fact that

references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). To support combining references, evidence of a suggestion, teaching, or motivation to combine must be clear and particular, and this requirement for clear and particular evidence is not met by broad and conclusory statements about the teachings of references. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Court of Appeals for the Federal Circuit has also stated that, to support combining or modifying references, there must be particular evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Furthermore, as affirmed by the Court of Appeals for the Federal Circuit in *In re Sang-su Lee*, a factual question of motivation is material to patentability, **and cannot be resolved on subjective belief and unknown authority**. See *In re Sang-su Lee*, 277 F.3d 1338 (Fed. Cir. 2002). Respectfully, as will be discussed below, the Official Action fails to meet the requirements for a prima facie showing of obviousness under § 103.

The Office Action notes that Kaken does not teach the specific conjugated estrogens set forth in Claim 32. The Action further alleges that Borah et al. teach that conjugated estrogen is useful in a pharmaceutical preparation for the treatment of osteoporosis. Applicants submit that Borah et al. merely shows a conjugated estrogen selected from "the group consisting of estrone, equilin, 17 $\alpha$ -dihydro-equilin, 17 $\alpha$ -estradiol, equilenin, 17 $\beta$ -dihydro-equilin and 17 $\beta$ -dihydro-equilenin". Claim 32 recites a mixture of estrogenic compounds, wherein said mixture comprises "salts of conjugated estrone, conjugated equilin, conjugated  $\Delta^{8,9}$ -dehydroestrone, conjugated 17 $\alpha$ -estradiol, conjugated 17 $\beta$ -dihydroequilin, conjugated 17 $\alpha$ -dihydroequilin, conjugated 17 $\beta$ -estradiol, conjugated equilenin, conjugated 17 $\alpha$ -dihydroequilenin, and conjugated 17 $\beta$ -dihydroequilenin". The presently claimed composition has different conjugated estrogens as compared to the Borah et al. reference. Furthermore, as noted in the Office Action, Kaken similarly fails to teach the specific conjugated estrogens as set forth in Claim 32. Borah et al. and Kaken also fail to

teach or suggest the use of a non-aromatizing androgen with an estrogenic compound. Accordingly, Applicants submit that there is no motivation to produce the pharmaceutical formulation as recited in independent Claim 32. Applicants submit that they are the first to discover the beneficial effects of using a non-aromatizing androgen with an estrogenic compound. Applicants point out that the Examples of the present specification illustrate that estradiol plus oxandrolone does not provide an additive effect and instead provides a reductive effect which shows that this combination is useful in treating hormonal deficiencies in women. There is nothing in Borah et al. or Kaken et al. which would make the present invention obvious. The composition as recited in Claim 32 and the composition in Borah do not possess a "similar utility." Therefore, Applicants submit that neither Borah et al. nor Kaken et al. teach or suggest the elements recited in Claim 32 of the present application. Applicants further submit that Borah et al. and Kaken fail to contain any motivation to combine their teachings as required by *In re Sang-su Lee*. Accordingly, Applicants respectfully request reconsideration of the rejection of Claim 32 under 35 U.S.C. § 103(a).

#### ENTRY OF AMENDMENTS

The amendments to the claims above should be entered by the Examiner because the amendments are supported by the as-filed specification and drawings and do not add any new matter to the application. Further, Applicants believe that the amendments do not raise new issues or require a further search. Applicants further submit pursuant to 37 C.F. R. § 1.116, amendments after final presenting rejected claims in better condition for allowance may be admitted.

#### CONCLUSION

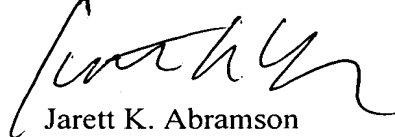
In view of the remarks presented herein, Applicants respectfully submit that the claims define patentable subject matter. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

It is not believed that an extension of time and/or additional fee(s)-including fees for net addition of claims-are required, beyond those that may otherwise be

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provided for in documents accompanying this paper. In the event, however, that an extension of time is necessary to allow consideration of this paper, such an extension is hereby petitioned under 37 C.F.R. §1.136(a). Any additional fees believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully Submitted,



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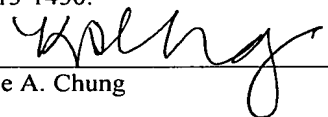
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